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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/516,075

11/29/2004

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EXAMINER

ZHENG, LI

ART UNIT

PAPER NUMBER

1638

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/516,075	Applicant(s) HERBERS ET AL.	
	Examiner LI ZHENG	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 11-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 November 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/29/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-20, and SEQ ID NO: 13-14 in the reply filed on 3/12/2008 is acknowledged. Non-elected subject matter must be removed from the claims.

As a result, claims 1-20 are pending.

Claim 10 is withdrawn for being drawn to non-elected invention.

Claims 1-9 and 11-20 are examined on the merits.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See, for example, page 23.

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3. The use of the trademarks "Bion®" and "Glyphosate®" have been noted in this application (pages 3 and 38). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

4. Claim 2-3, 9, 16 and 20 are objected to because the claims contain non-elected sequences.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-9 and 11-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A review of the full content of the specification indicates that obtaining nucleic acid sequences encoding any sucrose isomerase or sucrose isomerase with at least 40% homology with the sequence of SEQ ID NO: 14; or nucleic acid sequences which is degenerated to a nucleic acid sequence of that contain the sequence of SEQ ID No: 13; or nucleic acid sequences with at least 40% homology with the nucleic acid sequence of SEQ ID No: 13; or nucleotide sequences that hybridize with a complementary strand of SEQ ID NO: 13 or a functional equivalent or the fragment thereof is essential to practice the invention.

The specification teaches plant expression vector expressing heterologous sucrose isomerase (SEQ ID NO: 14 encoded by SEQ ID NO: 13) from *E. rhapontici* under the CaMV 35S promoter (p35S-cwlso) or under the promoter of the class I patatin gene (pB33-cwlso) or under feeding cell specific promoter (pLemmi9-cwlso or p Δ 0.3TobRB7-cwlso) (Examples 3, 4, and 8-9). The specification further discloses that transgenic potato plants expressing pB33-cwlso show markedly increased resistance to *Alternaria solani* (Example 7) and that transgenic potato plants expressing pLemmi9-cwlso or p Δ 0.3TobRB7-cwlso show markedly increased resistance to root-knot nematodes, *Meloidogyne incognita* (Examples 10-11).

The Applicants do not identify essential regions of the protein of SEQ ID NO:14, nor do Applicants describe any polynucleotide sequence that has at least 40% identity to SEQ ID NO:13, or any polynucleotide that encodes a protein having at least 40% identity to SEQ ID NO:14, or a functional equivalent or the fragment thereof, or nucleotide sequences that hybridize with a complementary strand of SEQ ID NO: 13,

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except for SEQ ID NO: 13 or 14. The specification does not teach conserved structures among the claimed genus that are essential for conferring disease resistance.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir.1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a sucrose isomerase falling within the scope of the claimed genus of polynucleotides which comprise nucleic acid sequences encoding sucrose isomerase with at least 40% homology with the sequence of SEQ IDNO: 14; or nucleic acid sequences which is degenerated to a nucleic acid sequence of that contain the sequence of SEQ ID No: 13; or nucleic acid sequences with at least 40% homology with the nucleic acid sequence of SEQ ID No: 13; or a functional equivalent or the fragment

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thereof, or nucleotide sequences that hybridize with a complementary strand of SEQ ID NO: 13. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the protein of SEQ ID NO: 14, it remains unclear what features identify a protein of SEQ ID NO: 14. Since said genus has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Scope of Enablement

6. Claims 1-9 and 11-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing resistance against *Alternaria solani* or root-knot nematodes, *Meloidogyne incognita*, by expressing nucleotide sequence SEQ ID NO: 13 encoding sucrose isomerase of SEQ ID NO: 14 under the control of pB33 promoter or feeding cell specific promoter in potato plant, does not reasonably provide enablement for a method of increasing resistance against any pathogen by expression of any sucrose isomerase or any variants of SEQ ID NO: 14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a plant expression vector comprising nucleic acid sequences encoding any sucrose isomerase or sucrose isomerase with at least 40% homology with the sequence of SEQ IDNO: 14; or nucleic acid sequences which is degenerated to a nucleic acid sequence of that contain the sequence of SEQ ID No: 13; or nucleic acid sequences with at least 40% homology with the nucleic acid sequence of SEQ ID No: 13; or a functional equivalent or the fragment thereof, or nucleotide sequences that hybridize with a complementary strand of SEQ ID NO: 13 under the control of a pathogen-inducible promoter, a method for generating resistance of a plant to pathogen by using the plant expression vector, and the transgenic plant produced.

The specification teaches plant expression vector expressing heterologous sucrose isomerase (SEQ ID NO: 14 encoded by SEQ ID NO: 13) from *E. rhapontici* under the CaMV 35S promoter (p35S-cwlso) or under the promoter of the class I patatin gene (pB33-cwlso) or under feeding cell specific promoter (pLemmi9-cwlso or p Δ 0.3TobRB7-cwlso) (Examples 3, 4, and 8-9). The specification further discloses that

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transgenic potato plants expressing pB33-cwlso show markedly increased resistance to *Alternaria solani* (Example 7) and that transgenic potato plants expressing pLemmi9-cwlso or pΔ0.3TobRB7-cwlso show markedly increased resistance to root-knot nematodes, *Meloidogyne incognita* (Examples 10-11).

The Applicants do not identify essential regions of the protein of SEQ ID NO:14, nor do Applicants describe any polynucleotide sequence that has at least 40% identity to SEQ ID NO:13, or any polynucleotide that encodes a protein having at least 40% or 95% identity to SEQ ID NO:14, or a functional equivalent or the fragment, except for SEQ ID NO: 13 or 14. The specification does not teach conserved structures among the claimed genus that are essential for conferring disease resistance.

The specification also fails to provide guidance in terms of how to make modifications to the SEQ ID NO: 14 to generate the claimed genus of variants that retain its disease resistant activity.

Falcon-Perez JM et al. (1999, *J Biol Chem.* 274:23584-90) teach that when twenty-two single amino acid substitutions or deletions were introduced into the nucleotide binding domains, the proposed regulatory domain, and the fourth cytoplasmic loop of the yeast cadmium factor (Ycf1p) vacuolar protein by site-directed mutagenesis, two conserved amino acid residues, Glu (709) and Asp (821), were found to be unnecessary for Ycf1p biogenesis and function.

The state of art also teaches that making “conservative” substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al. (1988, *Mol. Cell. Biol.* 8:1247-1252) teach that

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the “conservative” substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while “nonconservative” substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the “nonconservative” amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the “conservative” amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins would have at least 95% identity to the original protein.

Guo et al. (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2).

Therefore, the instant specification fails to provide guidance for which amino acids of SEQ ID NO: 14 can be altered, the type of alteration, and which amino acids must not be changed, to maintain disease resistant activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein.

Without further guidance, undue experimentation would have been required for a person skilled in the art to develop and evaluate nucleic acids encoding variants of polypeptide of SEQ ID NO: 14, wherein said polypeptide has sucrose isomerase and disease resistant activity. See *Genentech Inc. v. Novo Nordisk*, A/S (CA FC) 42

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USPQ2d 1001 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Further, regarding the nucleotide sequences that hybridize with a complementary strand of SEQ ID NO: 13, hybridization condition, which is essential to define the claimed nucleotide sequences, is not recited in the claims. Therefore, any DNA could hybridize to the sequence indicated by SEQ ID No.13 more or less at an appropriate condition.

Still further, the claims are drawn to a transgenic plant that displays increased resistance to any plant pathogens. However, the specification only teaches that transgenic potato plants expressing pB33-cwlso show markedly increased resistance to *Alternaria solani* (Example 7) and that transgenic potato plants expressing pLemmi9-cwlso or pΔ0.3TobRB7-cwlso show markedly increased resistance to root-knot nematodes, *Meloidogyne incognita*. Neither the specification nor the prior art teaches that when expressed in plant, the claimed peptides could confer increased disease resistance to any fungi, or any other plant pathogens which also include bacteria, viruses and insects. Veronese et al. (2003, *Plant Physiology* 131:1580-1590) teach that many plant antimicrobial proteins are toxic to some microbes but are ineffective against others (page 1582, last paragraph). Given the breadth of the claims, lack of guidance on the mode of action of the claimed antifungal peptide, undue experimentation would have been required to vigorously test the activity in vivo and in vitro against a significant number of pathogens that could reasonably represent all of the plant pathogens.

Given the claim breadth, unpredictability of the art, and lack of guidance as discussed above, undue experimentation would be required by one skilled in the art to practice the invention in full scope.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 8-9, 11-14 and 16-17 rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kunz et al. (04/04/2002, WO/2002/027003; Note: see US Patent Application Publication Number 2004/0064851 for English translation).

The claims are drawn to transgenic expression cassette comprising a nucleic acid sequence that encodes a sucrose isomerase in functional linkage with a pathogen-inducible promoter that is functional in plants; wherein the sucrose isomerase is a functional equivalent of the protein of SEQ ID NO: 14 or at least 40% homology with SEQ ID NO: 14; the transgenic expression vector comprising the expression cassette; the transgenic potato comprising the expression vector.

Kunz et al. teach binary vector comprising sucrose isomerase gene from *Protaminobacter rubrum* (SEQ ID NO: 1) under the control of B33 promoter. Kunz et al.

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further teach that *Agrobacteria* were transformed with the binary vector and that transgenic potato plants comprising the vector were obtained (paragraphs [0050]-[0051] and [0067]). According to the sequence search, SEQ ID NO: 1 of Kunz et al. encodes a sucrose isomerase that shares 84% identity to SEQ ID NO: 14 of instant invention (See alignment attached) and is considered as a functional equivalent of the protein of SEQ ID NO: 14.

Claims 8-9, 11-14 and 16-17 require plant promoter be pathogen-inducible. Kunz teaches the plant promoter from patatin B33 gene as claimed in the instant application but does not mention the characteristic or property of being pathogen inducible as claimed. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. However, the same promoter is used in the instant invention to generate transgenic potato plant resistant to *Alternaria solani*. See *In re Best* 195 USPQ 430, 433 (CCPA 1977). The examiner is not in a position to make a conclusion of “inherency/anticipation” or “obviousness” since the record does not allow one to determine if and how the claimed subject matter differ from the prior art. Accordingly, the burden shifts to the Applicant to provide evidence that the prior art neither anticipates nor renders obvious the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Anne Marie Grunberg/
Supervisory Patent Examiner, Art Unit 1638

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